Central New York Regional Poison Control Center

January 1996

The CNYPCC Toxicology Letter

A Quarterly Publication

SCHEDULED EVENTS:

S.U.N.Y., H.S.C. Department of Emergency Medicine
Emergency Medicine Grand Rounds
Marley Education Center: Sulzle Auditorium
Third Friday of the Month, 11:00 AM

Jan.19	Challenges in Pediatric Sedation & Analgesia
Feb.16	Toxicology - When ACLS is not enough

Toxicology Case Conference
CNYPCC, 550 E Genesee Street
Poison Center Conference Room
Every Thursday, 11:00 AM - 12:00 PM

HISTORICAL TIDBITS:

1. What toxin was responsible for Ginger Jake Paralysis?
   Hint: it was a contaminant in liqueur production during prohibition.

2. Elixir of sulfinalamide was responsible for what epidemic in 1937?

Answers on back page

Introduction

The Central New York Poison Control Center (CNYPCC) is pleased to provide you with the first issue of "The CNY Toxicology Letter". Published quarterly, this newsletter will be distributed to all the Emergency Departments and Critical Care Units within our 14 county service area. Designed for health care professionals, the letter will discuss issues specifically directed to the evaluation and management of the poisoned patient. As further issues are generated, we hope to encourage suggestions from our audience on design and content. To that end, please feel free to contact the CNYPCC at the address and phone number listed at the end of this newsletter.

CASE HISTORY

ANESTHESIA EMERGENCY

A 29 year old female complaining of lower back pain is to receive a trigger point injection of 10 mL of 0.75% bupivacaine. A needle was inserted, and after a negative aspiration for blood the drug was administered. After 1-2 minutes, she complained of nausea and 2 minutes later she had a witnessed cardiac arrest. Standard advanced cardiac life support with cardiopulmonary resuscitation was initiated, and after a prolonged resuscitation, the patient was stabilized.

What is bupivacaine?

Bupivacaine is a local anesthetic of the amide class. Examples of other local anesthetics of the amide class include mepivacaine and lidocaine. Bupivacaine has a long duration of action, with the onset of nerve block occurring in 4-7 minutes and lasting for 4-7 hours. It is highly protein bound and is eliminated principally through hepatic metabolism. Bupivacaine is used for peripheral, sympathetic and epidural block anesthesia.

What is the toxicity from bupivacaine and how does it compare to mepivacaine and lidocaine toxicity?

Toxicity from all local anesthetics includes both cardiac and central nervous system effects. These effects are due to a high local concentration of the drug, and generally occur only after a high dose of the drug has been inadvertently given or a therapeutic dose of the drug has been given too quickly. Cardiac effects are due to the drug's class IB antidysrhythmic effect which slows phase 4 automaticity and may result in sinus arrest, AV block, hypotension, ventricular dysrhythmias and cardiac arrest. Central nervous system effects include drowsiness, weakness, euphoria, dysphoria, paresthesias, muscular fasiculations and seizures. Lidocaine toxicity typically results in seizure activity before the onset of its myocardial depressant effects, whereas bupivacaine and mepivacaine may produce cardiac effects simultaneously with CNS effects. Also, as is the case with this patient, cardiac effects of bupivacaine may occur without any CNS effects at all.

If a patient is allergic to one local anesthetic are they allergic to all of them?

There are currently two types of local anesthetics available; the ester containing and the amide containing local anesthetics. The allergy associated with amide anesthetics (ie. lidocaine, bupivacaine, mepivacaine) is generally due to the drug's preservative. True allergy to the amide drugs is possible, however it is rare and limited to the specific agent responsible.

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Therefore, a patient with an allergy to one amide can safely be given either another amide local anesthetic or an ester anesthetic if it does not contain the same preservative.

The ester anesthetics are different. Some of the agents included in this group are cocaine, procaine, benzocaine and tetracaine. These agents are metabolized to a common product, para aminobenzoic acid (PABA). Allergy to any of these agents is due to an allergy to this metabolite. Thus, after an allergic reaction to one agent in the ester class occurs, the use of another agent in this class is likely to result in cross-allergenicity. In these cases, it would be prudent to switch to an agent of the amide class for future local anesthetic use.

An easy way to remember these groups is that the common amide group local anesthetics contain two i's in their name where the common ester group local anesthetics contain only one i in their name.

How can we protect patients from receiving inadvertent intravascular administration of anesthetics?

Prior to the injection of a local anesthetic in a peripheral site, it is generally recommended to check for possible entry in a vascular structure by ensuring that there is no blood return on aspiration. This should be done in all cases, however, as in this case it may not be adequate for several reasons. First, aspiration in a small vein may temporarily collapse the vein, resulting in a negative aspiration. Also, a vein may become lacerated as a needle passes through it. This may result in a negative aspiration because the needle is actually in the vein, but the needle opening is outside the vein. The drug enters the vein through passage that is left after the needle is withdrawn.

How is local anesthetic toxicity treated?

This patient probably received an intravenous bolus of bupivacaine instead of a peripheral nerve injection. The resultant increased vascular concentration produced myocardial toxicity. Treatment available for these patients is limited. Seizures should be treated with supportive care and benzodiazepines. Cardiovascular toxicity should be treated with advanced cardiopulmonary resuscitation. The use of hyperventilation and/or sodium bicarbonate has been proposed for the treatment of sodium channel blockade. This may have some role and should be tried for cardiovascular effects induced by these agents.

The length of toxicity is dependent on the time the drug is in contact with the affected organs. Lidocaine redistributes to the periphery quickly and toxicity is usually limited to minutes. However, the cardiodepressant effects from other local anesthetics can be prolonged. Bupivacaine and mepivacaine induced cardiopulmonary arrest is usually long lasting and prolonged resuscitation measures and bypass are often required and are still frequently unsuccessful. When patients survive, they occasionally are left with neurological deficits. This patient was unfortunately left with severe neurological defects requiring ventilatory support.

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Thomas RD, Behbehani MM, Coyle DE, Denson DD. Cardiovascular toxicity of local anesthetics: an alternative hypothesis. Anesth Analg. 1986;65:444-50.

Rosen MA, Thigpen JW, Shnider SM, Foutz SE, Levinson G, Koike M. Bupivacaine-induced cardiotoxicity in hypoxic and acidotic sheep. Anesth Analg. 1985;64:1089-96.

Feldman HS, Arthur GR, Pitkanen M, Hurley R, Doucette AM, Covino BG. Treatment of acute systemic toxicity after the rapid intravenous injection of ropivavaine and bupivacaine in the conscious dog. Anesth Analg. 1991;73:373-84.2

TOX TRIVIA:

1. What is the #1 toxin related cause of death in the United States?
2. What is the toxic effect of shoe desiccants (silica gel)?
3. What is the toxin that is contained in jimson weed?
4. Why is freezing point depression the preferred method for determining osmolality in toxic alcohol poisoned patients?

CLINICAL TOXICOLOGY PEARLS:

1. Any salicylate exposed persons urine will turn violet purple when a few drops of 10% ferric chloride solution is added to it.
2. Fetal hemoglobin reads as carboxyhemoglobin on a co-oximeter.
3. The blood of a patient with methemoglobinemia will appear brown.

Historical Tidbits answers:

1. tri ortho cresyl phosphate (TOCP)
2. renal failure (the elixir's diluent was diethylene glycol)

Tox Trivia answers:

1. carbon monoxide
2. it is non-toxic
3. datura stramonium (anticholinergic toxicity)
4. Because if boiling point elevation is used, all the alcohol would volitize off first.

Central New York Regional Poison Control Center

April 1996

The CNYPCC Toxicology Letter

Vol. 1 No. 2

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SCHEDULED EVENTS:

S.U.N.Y., H.S.C. Department of Emergency Medicine
Emergency Medicine Grand Rounds
Marley Education Center: Sulzle Auditorium
Third Friday of the Month, 11:00 AM

April 19	Rational Use of Antibiotics in the Pediatric Ed.
May 17	Emergency Toxicology
June 21	Evaluation of the Acute Scrotum

Toxicology Case Conference
CNYPCC, 550 E Genesee Street
Poison Center Conference Room
Every Thursday 11:00 AM - 12:00 PM

HISTORICAL TIDBITS:

1. The Borgia family were famous poisoners, utilizing _____ and _____ as favorite weapons.

2. The toxin that devastated Minamata Bay, Japan, producing congenital defects in children born to women eating the fish was?

3. How did the basketball player Len Bias die?

Answers on back page

CASE HISTORY

AM I BLUE?

A ten month old previously healthy infant presents with cyanosis. His parents state that over a four hour period, while at play, they noted him to become "bluer and bluer." He has been well during the past few days, without cough, fever, change of behavior, or known contacts. His past medical history is essentially negative. He takes no medications.

On presentation the infant is afebrile with a respiratory rate of 30. His heart rate is 120 and regular. There is no work of breathing noted. His capillary refill is two seconds. He has peripheral and central cyanosis. His blood pressure is 90/50. His lungs are clear and no murmurs are noted on exam. His abdomen is soft, non-tender, without mass. Full peripheral pulses are palpable. He is neurologically intact.

What immediate interventions are indicated at this point?

Since the infant is cyanotic, 100 percent oxygen by mask should be administered. In addition, the patient should be placed on a cardiac monitor to determine whether any arrhythmia is present. Intravenous access should be obtained as well. Peripheral oxygen saturation may be obtained by the use of an oximeter at the bedside.

What is the differential diagnosis of cyanosis in infancy?

When evaluating an infant with cyanosis out of the newborn period (0-28 days), the clinician is advised to consider the physiologic function of three organ systems, namely the cardiac, pulmonary, and hematologic systems. With regard to the likelihood of acute cyanotic pulmonary events, consideration should be given to the potential for foreign body aspiration, acute bronchospasm, or the presence of a spontaneous pneumothorax. In this case, however, the absence of significant respiratory distress diminishes the likelihood of these pulmonary entities.

Infants born with cyanotic cardiac lesions will most often present within the first ten days of life with cyanosis and/or respiratory distress. The five most common cyanotic cardiac lesions include Tetrology of Fallot, Transposition of the Great Vessels, Truncus Arteriosus, Tricuspid Atresia, and Total Anomalous Pulmonary Venous Return. Since this child's past medical history was unremarkable, it is unlikely that an unknown cyanotic cardiac lesion would first present at 10 months of age.

The ability of hemoglobin to carry oxygen may be impaired in certain situations. Exposure to carbon monoxide in sufficient quantities will displace oxygen from the hemoglobin molecule. An additional impairment to the oxygen carrying capacity of hemoglobin would be a situation where the iron molecule within hemoglobin is changed from the ferrous to the ferric state, namely methemoglobinemia.

How can the laboratory assist in making a diagnosis in this case?

All patients presenting with cyanosis should undergo radiographic evaluation of the chest. In this scenario the chest film demonstrated a normal cardiac silhouette, with clear lung fields and the absence of the pneumothorax. An ECG should also be obtained to rule out structural anomalies of the heart. In our patient, the ECG was unremarkable. An arterial blood gas demonstrated a PH of 7.43, a PCO2 of 36, and a PO2 of 385. The oxygen saturation measured at the bedside was 90 percent. Precise measurement by a co-oximeter within the laboratory concomitant with the ABG revealed an oxygen saturation of only 70 percent. In addition, some drops of blood were spilled during the arterial puncture, which were brown in color, signifying the presence of methemoglobin.

What is the diagnosis in this case?

The scenario of cyanosis unresponsive to supplemental oxygen in the absence of cardiopulmonary compromise should alert the clinician to the presence of an abnormal hemoglobin oxygen transport system, i.e. methemoglobinemia. In addition, the conversion of red blood to a brown color when exposed to room air also points to this diagnosis as well.

What is methemoglobinemia?

Methemoglobinemia represents the clinical presentation of cyanosis and other findings consistent with asphyxia relative to the conversion of iron from the ferrous to ferric state.

When converted, the iron is incapable of binding oxygen and therefore will not deliver oxygen to the periphery.

Methemoglobinemia may be caused by three essential mechanisms:

a. Hereditary presence of an abnormal hemoglobin (hemoglobin M).
b. Hereditary deficiency of naturally occurring methemoglobin reductase.
c. Exposure to oxidant drugs or chemicals.

Of the aforementioned entities, the last category represents the etiology of most methemoglobinemia cases.

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What chemicals or drugs have been reported to cause methemoglobinemia?

There are many medications and chemical agents that are known to cause methemoglobinemia, as summarized in the tables below:

MEDICATIONS

Amyl Nitrate	Nitroprusside
Benzocaine	Phenacetin
Dapsone	Prilocaine
Lidocaine	Quinones
Nitroglycerin	Sulfonamides

CHEMICAL AGENTS

Aniline Dyes (shoe dyes, marking inks)	Napthalene
Chlorobenzene	Nitrophenol
Fires	Nitrous Gases (arc welders)
Isobutyl Nitrite	Trinitrotoluene
Foods with Nitrites or Nitrates	Well Water (nitrates)

Both nitrates and nitrites have been reported to convert iron to the ferric state. Nitrates may be found naturally in nature in contaminated well water. Infants with severe diarrhea may proliferate nitrates within their small and large bowel and may present with methemoglobinemia as well. Nitrates dispensed for the control of angina have also been implicated. Napthalene, contained in moth balls, is an additional etiologic agent. Illicit use of inhaled nitrates (known as "whippits") has also been implicated in cases.

Topical anesthetics such as Benzocaine and Lidocaine have been implicated in methemoglobinemia cases presenting in infancy. These agents are available as OTC topical anesthetic agents for the relief of dental pain during teething.

What are the symptoms of methemoglobinemia?

In previously healthy individuals, methemoglobin concentrations of 10-20% usually result in cyanosis without apparent clinical manifestations. At 20-50%, dizziness, fatigue, headache and exertional dyspnea may develop. Lethargy and stupor usually appear at about 50%, and the lethal concentration is probably greater than 70%.

What is the treatment for methemoglobinemia?

The recommended therapy for methemoglobinemia is the intravenous administration of Methylene Blue, 1-2 mg/kg, as a 10% solution (0.1-0.2 cc/kg) over five minutes. Clinical response is often immediate with resolution of the cyanosis. Treatment failures have been known to occur in patients who have not been decontaminated relative to their exposure (especially in cases involving Dapsone). It is important to realize that in oral exposure, the administration of activated charcoal may be necessary to facilitate decontamination. In addition, Methylene Blue may be ineffective and induce varying degrees of hemolysis in patients who are deficient in Glucose-6-Phosphate Dehydrogenase. Deficiency of this enzyme has been reported to occur in 200 million people worldwide, with the highest incidence in the US amongst African-Americans (11%). Degrees of deficiency vary, however, from mild (African-Americans) to severe (Greeks and other Mediterranean groups). These patients will, if exposed to Methylene Blue, not only remain cyanotic but will also undergo rapid hemolysis when exposed to this agent. It is therefore important to obtain accurate histories before administering Methylene Blue.

Treatment failures with Methylene Blue may be seen in patients with sulfhemoglobinemia. Many of the drugs and chemicals that produce methemoglobin will also produce sulfhemoglobin, a compound that also produces cyanosis in affected patients. When analyzed spectrophotometrically, it is indistinguishable from methemoglobin, which may add confusion to the diagnosis. Resistant to methylene blue, its major mechanism of destruction occurs upon death of the red cell itself. Fortunately, it shifts the oxyhemoglobin curve to the right, facilitating the delivery of oxygen to the tissues.

Additional causes of treatment failure with Methylene Blue include patients with Hemoglobin M disease and NADPH Deficiency.

How reliable is pulse oximetry in evaluating patients with methemoglobinemia?

Pulse oximeter saturation determinations are not accurate when blood contains methemoglobin. Oximeters are calibrated only to read oxyhemoglobin and deoxyhemoglobin species accurately in pulsatile blood. Methemoglobin interferes with these readings in a complicated fashion. It is therefore recommended that oxyhemoglobin measurements be performed in the laboratory by the use of a cooximeter. Arterial blood sampling will also provide precise measurement of methemoglobin levels.

What was the outcome of this case?

The infant's methemoglobin concentration was 18%. Treatment with methylene blue resolved all symptoms within 4 hours. Overnight observation in the hospital was unremarkable. Further history revealed daily use of Orajel, a topical teething medication, which contains benzocaine.

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Layne WR et al. Methylene blue uptake and the reversal of chemically induced methemoglobinemia's in human erythrocytes. J. Pharmacol Exp Ther. 1969; 165: 36-43.

Rosen et al. Failure of methylene blue treatment in toxic Methemoglobinemic. Ann Int Med. 1971; 75:83-86

TOX TRIVIA:

1. What was the name of the NSAID that was withdrawn from the pharmaceutical market due to a high incidence of anaphylactic reactions?

2. What is the odor that is associated with cyanide poisoning and what is the compound that produces the odor?

3. How much commercial ground nutmeg would be required to be ingested to cause psychoactive effects?

4. Etoposide is a synthetic analog of?

CLINICAL TOXICOLOGY PEARLS:

1. 6 hours non-toxic???? What clinical finding should be absent for this statement to be true for the following toxins? a. tricyclic antidepressants b. iron

2. If a patient is cyanide poisoned, the arterial blood gas will not improve after supportive care.

3. Sulfhemoglobin is read as methemoglobin on a co-oxymeter. Add cyanide to sulfhemoglobin and the interference will be diminished.

Historical Tidbits Answers:

1. arsenic and phosphorous
2. methyl mercury
3. cocaine poisoning

Tox Trivia Answers:

1. zomipirax
2. bitter almond and amygdalin
3. Two Tablespoons Full
4. podophyllline

Clinical Toxicology Pearls Answers:

1. a. tricyclic antidepressants = electrocardiogram changes (QRS > 100 msec)
   b. iron = vomiting

Central New York Regional Poison Control Center

The CNYPCC Toxicology Letter

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SCHEDULED EVENTS:

S.U.N.Y., H.S.C. Department of Emergency Medicine
Emergency Medicine Grand Rounds
Marley Education Center: Sulzle Auditorium
Third Friday of the Month, 11:00 AM

July 19	Pediatric Surgical Emergencies
August 16	Genitourinary Problems in the Emergency Department
September 20	CPR: Where We Were, Where We Are, and Where We Are Going

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NEWS BULLETIN:

On April 10, 1996 the FDA issued a warning about the product "Herbal Ecstasy". This product has been associated with over 100 reports of adverse effects, including 15 deaths. The active ingredient is ephedrine and may also be listed as Ma Huang, ephedra sinica or ephedra extract.

CASE HISTORY

VACATION EMERGENCY

A 29 year old female is brought to the Emergency Department with a 3 day history of increasing lethargy, weakness, difficulty swallowing and left hand parasthesias. Three days prior to admission, while vacationing in Florida, the patient swam in a "red tide" and had also eaten a large amount of Sheephead and Yellowjack fish caught from the ocean. Approximately 12 hours after eating, she experienced shortness of breath, mild chest pain, and tingling left hand digits. These symptoms increased in severity until the day of admission where she was unable to lift her 15 month old daughter.

The patient's past medical history is non-contributory. Physical examination reveals a well developed, well nourished woman in no apparent distress. Significant physical examination findings include a blood pressure 120/60 mm Hg, pulse 98 bpm, temperature 37.1 C and respiratory rate 20 bpm. There is mild generalized abdominal tenderness without rebound or guarding. On neurologic assessment, she is alert and orientated to person, place, and time. Reflexes are 2+ in the upper and 4+ in the lower extremities. Motor strength is 5/5 throughout. There is a decrease in left hand light touch perception in the distribution of C6 and C7. During the first day of hospitalization, the patient develops perioral tingling and tingling of the tongue. Gait was normal and no nystagmus was present. Laboratory tests include a Na 144 meq/L, CL 96 meq/L, K 3.9 meq/L, HCO3 25 meq/L, Ca of 10 meq/L, PO4 3.7 meq/L. Renal and hepatic function studies are normal. Also uric acid, albumin, CBC, ESR and UA are all within normal limits. Chest radiograph, electrocardiogram and MRI are read as normal.

What is this patient's differential diagnosis?

There are several causes of acute neurologic dysfunction. This patient gives a history of exposure to the "Red Tide" and to seafood that the patient obtained while fishing that same day. We will limit our discussion to toxins associated with her exposure.

What is the "Red Tide"?

During the non "R" containing months of the year (May through August) plankton proliferate through photosynthesis in warm areas of the world. This phenomena occurs on both the East and West coast of the United States and generally occurs between 30 degrees North and South latitude of the equator. These plankton belong to the phylum Protozoa and are single celled pigmented organisms. Shellfish feed off these dinoflagellates and bioconcentrate their toxin. Subsequent ingestion of these shellfish may cause neurotoxic, paralytic or amnestic symptoms. If large numbers of dinoflagellates are present, walking down a beach that is infested with the red-tide may produce bronchospasm due to aerosolized toxin. The most frequently implicated dinoflagellates include Ptychodiscus brevis [neurotoxic], Prototgonyaulax catanella and Prototgonyaulax tamarensis [paralytic], and Nitzschia pungens [amnestic]. The neurotoxic dinoflagellate produces the toxin brevitoxin, while the paralytic dinoflagellate produces saxitoxin. The amnestic shellfish poison is thought to be domoic acid.

All the toxins associated with the red-tide are heat insensitive. The onset of symptoms associated with the red tide is usually within 30 minutes to several hours after exposure. Neurotoxic shellfish poisoning from brevitoxin may appear 15 minutes to 18 hours (usually 3 hours) after exposure as "hot-cold inversion of sense", myalgias, nausea, vomiting, diarrhea, bradycardia, decreased reflexes and dilated pupils. Brevitoxin also increases sodium flux in bronchioles and may result in bronchoconstriction. Symptoms usually resolve within a day after exposure with a range of 1 to 72 hours

Paralytic symptoms from saxitoxin usually begin approximately 30 minutes after exposure and may include perioral or extremity parathesias, headache and ataxia, which may progress to paralysis and cranial nerve dysfunction. Death is usually due to respiratory failure and occurs within 12 hours of exposure.

Amnestic shellfish poisoning may have a delay in onset of about 5 hours (15 minutes to 38 hours) and is heralded by gastrointestinal symptoms such as nausea, vomiting, and diarrhea followed by memory loss. Rarely, more severe neurologic symptoms of coma, seizures, and hemiparesis may occur. The suspected toxin, domoic acid, may interact with NDMA receptors as it is a structural analog of glutamic and kainic acid. These excitatory amino acids are currently being researched for their possible role in causing neuronal cell death.

Treatment for red-tide poisoning is supportive, with special attention to airway and respiratory support. Gastrointestinal decontamination should be considered in symptomatic individuals. It is unlikely that our patient was poisoned through contact with the red-tide. Her exposure would have been to aerosolized toxin and should have resulted in respiratory symptoms which did not occur. Also, the timing of her symptoms was relatively late for brevitoxin, starting at 12 hours and lasting for 3 weeks. Upon questioning, we also learned that several other family members also went swimming in the red-tide without clinical effect so we considered this an unlikely etiological agent for this patient's symptoms.

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What is the differential of fishborne poisoning?

There are many toxins that are associated with the ingestion of fish products. The large differential can be narrowed by determining the type of fish ingested, the area in the world where the person obtained the fish and the signs and symptoms of toxicity that the patient is experiencing. Our patient was in Florida, caught her own fish and ate it. This excludes many exotic fish-borne illness that would be a consideration in other areas of the world. It does however, leave several options to consider.

Scombroid poisoning is a common type of fish poisoning that occurs with the improper refrigeration of fish. Fish most often associated with the production of toxin leading to scombroid poisoning include albacore, bluefin and yellowfin tuna, dolphin, sardine, anchovy, herring and bluefish. During periods of non-refrigeration, the musculature of these fish undergoes decomposition. Bacteria (classically *Morganella morganii*) decarboxylate the amino acid l-histidine to histamine and saurine (histamine hydrochloride). Affected fish may have a metallic or peppery taste. Symptoms usually develop within 15-90 minutes after exposure and include flushing, pruritis, urticaria, angioneurotic edema, bronchospasm, nausea, vomiting, headache, tachycardia and hypotension. Treatment consists of supportive care and antihistamines. Outcome is generally favorable with symptoms resolving within 8 to 12 hours.

Tetrodotoxin is a fish poison within the specific fish order Tetrodontiformes. Examples of fish containing tetrodotoxin include the pufferfish (toadfish, blowfish, globefish, swellfish, baloonfish) and porcupine fish. Tetrodotoxin is thought to be identical to the toxin tarichatoxin which is found in North American and Chinese newts, International salamanders, the skin of the Central American frogs (genus Atelopus), some shellfish, the Ribbon worm, Flat worm, Horseshoe crab and the Blue Ringed octopus. The toxin is an amino-perhydroquinazolone and is found throughout the fish with highest concentrations in the liver, gonads, intestine and skin. The mechanism of toxicity is the blocking of sodium channels at the level of the axon. Symptoms, after exposure to tetrodotoxin can occur in as little as 10 minutes, but can be delayed for up to 4 hours. Initially, the patient may present with perioral parasthesias, lightheadedness, generalized parasthias, nausea, vomiting, weakness. An ascending paralysis may develop with death occurring in 6-24 hours. Other symptoms that may occur include seizures, hypersalivation, diaphoresis, and ataxia. Mentation may be maintained despite flaccid paralysis. Survival past 24 hours is considered a good prognostic sign.

Ciguatera toxin is usually found in fish that live between the 35th degree North and South latitude. These fish are usually bottom dwelling Reef fish, and poisoning usually occurs in the Spring and Summer months. Large fish (greater than 6 pounds) and older fish bioaccumulate the toxin as they ingest smaller herbivorous fish that extract the dinoflagellate Gambierdiscus toxicus from blue-green algae. Many species are implicated in causing ciguatera poisoning. These include mullets, groupers, snappers, parrot fish, amberjack and barracuda. Symptoms of ciguatera occur within 1-3 hours after ingestion and include abdominal pain, nausea, vomiting, diarrhea, chills, parathesias (perioral, classic "hot/cold" dissociation), a metallic taste, and pruritis. Rarely, the patient's course may progress to respiratory failure and death. The gastrointestinal symptoms generally resolve in 24-48 hours, but the neurologic symptoms may remain for several days to weeks often correlating with the amount of toxin ingested.

This patient ate Sheaphead and Yellowjack, developed perioral and limb parasthesias that developed 12 hours after exposure and lasted 3 weeks post-exposure. These signs and symptoms are most consistent with ciguatera poisoning.

How can we prove that that this patient has ciguatera poisoning?

ELISA (enzyme linked immunoabsorbent assay) tests for ciguatera toxin can be done, but are not available in most institutions. Most likely, this diagnosis will be a diagnosis of exclusion.

What are the possible treatments for ciguatera poisoning?

The treatment of a patient exposed to ciguatera is largely supportive. If the ingestion was recent and thought to be in the stomach, there may be some benefit to syrup of ipecac. Later, activated charcoal may help bind toxin that is not yet absorbed. Intravenous mannitol has been reported to reverse the neurologic findings associated with ciguatoxin poisoning at a dose of 1 g/kg over 45 minutes. Mannitol should always be used carefully with consideration to the patient's fluid and electrolyte status. Many other agents have been proposed for treatment of ciguatera poisoning including pralidoxime, amitriptyline, corticosteroids, and calcium, none achieving convincing success.

Our patient received supportive care and her symptoms spontaneously resolved over the next several weeks.

Contribution: Maxwell P, Stork C.

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MMWR. Tetrodotoxin poisoning associated with eating puffer fish transported from Japan - California, 1996. 1996;45(19):389-391.

TOX TRIVIA:

1. What household toxin is associated with blue green vomitus and lobster red skin?
2. What rodenticide is associated with a rotten fish odor?
3. The may apple is a plant associated with which toxin?
4. The type and character of "anticholinergic" hallucinations are?

CLINICAL TOXICOLOGY PEARLS:

1. Heavy metals are radiopaque and may be seen radiographically after acute poisoning.

HISTORICAL "MATCHING" TIDBITS:

1. Vitus Guerulitas (Tennis Player)	a. amyl nitrate
2. Paul Lynde (hollywood squares)	b. CN
3. John Belushi	c. speedball (heroin/cocaine)
4. Jonestown Massacre	d. CO

Historical "Matching" Tidbits Answers:

1. d 2. a 3. c 4. b

Tox Trivia Answers:

1. Boric acid in large amounts
2. Zinc Phosphide
3. Podophyllline
4. Visual - Lilliputian (they see imaginary objects as being smaller than they are)

Central New York Regional Poison Control Center

The CNYPCC Toxicology Letter

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SCHEDULED EVENTS:

S.U.N.Y., H.S.C. Department of Emergency Medicine
Emergency Medicine Grand Rounds
Marley Education Center: Sulzle Auditorium
Third Friday of the Month, 11:00 AM

Oct. 18	Pediatric Emergency Medicine Update
Nov. 15	Renal Transplant Emergencies
Dec. 20	Best Cases of the Year

Toxicology Case Conference
CNYPCC, 550 E Genesee Street
Poison Center Conference Room
Every Thursday 11:00 AM - 12:00 PM

HISTORICAL "MATCHING" TID BITS:

1. Chimney sweeps	a. oxides of nitrogen
2. Meat packers asthma	b. scrotal cancer
3. Silo fillers disease	c. Polycyclic aromatic hydrocarbons
4. Hearing loss in hairdressers	d. bromates

Answers on back page

CASE HISTORY

BEWARE THE "FASCINOMA"

CASE ONE: FACTITIOUS HYPOGLYCEMIA

A 2 year old male arrived in an unresponsive state. He was said to be unarousable after his regular afternoon nap. Recent trauma and medication use were denied.

Physical examination revealed a comatose child with absence of purposeful responses. Vital signs were normal, with the exception of mild tachycardia. Pupils were midposition, equal and reactive. Fundi were normal. There was generalized increase in muscle tone with intermittent decerebrate posturing. Deep tendon reflexes were preserved.

Laboratory analysis: blood glucose of 22, electrolytes otherwise normal. Tests of urine, serum, and gastric aspirates were negative for salicylates, APAP, alcohol, and oral hypoglycemics. A skeletal survey showed a healed fracture of the left radius and ulna.

An IV was begun, a bolus of D25W was given, and a continuous infusion of D5W begun. Interventions included augmented glucose support to D20W and steroids, with eventual normalization of blood sugar. After 20 hours, this ancillary support was withdrawn, with no fall in serum glucose levels. Full neurologic recovery was noted. Serum insulin and C-peptide levels drawn at 2, 4, and 12 hours, and at 2 and 4 months post discharge demonstrated a hyperinsulinemic state which had resolved after discharge from the hospital.

Additional history demonstrated the presence of the mother's boyfriend who was also an insulin dependent diabetic. Full disclosure was obtained from the boyfriend/perpetrator after social service investigation.

CASE TWO: CHRONIC DIARRHEA AND FAILURE TO THRIVE

A 23 month old female was admitted for the fifth time with a chief complaint of vomiting and diarrhea. The child lived at home with her mother who was separated from the father. History was positive for 10 to 15 watery stools every day since infancy. The patient was pale and irritable, with growth parameters clearly demonstrating a decline from the 50th to 5th percentile for weight. During each of her hospitalizations, the child had watery, pink tinged stools that averaged 250 grams per day.

Extensive laboratory analysis was normal for: CBC, ESR, urinalysis, immune status, stool cultures, upper GI imaging, barium enema, urine catecholamines, and 72 hour fecal fat content. A small intestinal biopsy was normal as well.

Alkalinization of multiple stools with sodium hydroxide showed a pink color change, suggesting the presence of phenolphthalein. The mother, when confronted with the cause of the patient's diarrhea, angrily denied giving laxatives. The child was placed in foster care, with close follow-up demonstrating normal catch-up growth and normal stool patterns.

CASE THREE: RECURRENT VOMITING, MUSCLE WEAKNESS, RHYTHM DISTURBANCES

A 16 month old male was evaluated at 9 months of age with vomiting, diarrhea, and poor weight gain. Results of stool examinations, abdominal ultrasound, and upper GI series were normal. The mother kept a daily log of foods that had precipitated the vomiting and diarrhea, with no clear pattern noted. The mother was described by the referring physician as a caring and involved parent. A 3 year old sibling was in good health.

Prior to evaluation, the child had demonstrated only a 500 gram weight gain over the prior three months. Upper GI endoscopy revealed a normal esophagus, stomach, and duodenum. A trial period wherein the child received only elemental formula failed to alleviate the vomiting or provide a substantial weight gain.

The vomiting and diarrhea continued with the child being hospitalized multiple times at different regional hospitals for dehydration. Premature ventricular contractions were noted. In addition, generalized muscle weakness developed, resulting in loss of ability to sit, stand, or walk.

Physical examination revealed a thin child with weight at the 5th percentile, height at the 75th percentile. He had marked muscle weakness, more prominent proximally. Head control was poor, and he could not stand or sit without support. The remainder of the neurologic exam was normal. Multiple PVC's were noted as well.

Abnormal laboratory values included a CPK of 3,307. ECG revealed PAC's and PVC's. An echocardiogram was normal. EMG and nerve conduction studies were normal. Ipecac poisoning was suspected and confirmed by the presence of emetine in the serum and urine. The mother was unable to provide any explanation.

The child was placed in foster care, whereupon the vomiting ceased and weight gain returned to normal. His motor strength gradually returned and his CPK returned to normal.

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CASE REPORT: EXCESSIVE VAGINAL BLEEDING

A 16 year old female presented to the Emergency Department, over a period of 6 months, four times with excessive vaginal bleeding during her menstrual cycle. Repeated gynecological examinations failed to reveal any anatomic abnormalities. Evaluation by the hematology service demonstrated, on each admission, a prolonged PT and evidence of vitamin K responsive clotting correction. Liver functions were normal. On two occasions, transfusions were necessary to correct her anemia. After admission to the adolescent service, the patient would receive vitamin K injections that would, at the time, fully correct her clotting abnormalities. Interadmission outpatient testing consistently demonstrated normal clotting functions. The patient and her family denied any prescription of non prescription drug use. School absences were plentiful yet her home tutoring performance was well above average. She was an only child. There was no family history of hematologic problems. In most instances, her Emergency Department stay was brief consisting of blood drawing, intravenous access, and rapid admission to a previously arranged inpatient bed.

On one occasion, the hematology attending, while writing her admission note in the Emergency Department, verbalized his frustration in arriving at an adequate explanation for her intermittent clotting abnormalities. Blood had been drawn on multiple occasions and analyzed for clotting factor deficiencies. Results were negative. In addition, serum was also tested for the presence of toxins that would contribute to clotting abnormalities. These tests were also negative. During one Emergency Department visit, the ED attending noted that the mother demonstrated a strong desire to have her child undergo a hysterectomy which would "cure her once and for all" of her bleeding problems. Investigation of the family demographics revealed that the mother worked at the hospital laboratory where the serum samples had been sent for toxin analysis.

On the basis of this, and after further discussion and investigation, paired serum samples were sent to both the mother's lab and an independent lab. Independent laboratory testing revealed the presence of exogenous levels of coumadin present in the child's blood. The sample sent to the mother's laboratory tested negative. On the basis of these findings, the child was removed from the home and Social Service investigation was instituted.

These cases, and others in the literature, represent a clinical scenario referred to as Munchausen Syndrome By Proxy (MSBP). The origin of Munchausen Syndrome refers to Baron Munchausen, an 18th century mercenary who went to battle with the Turks. On the basis of his writings, which later proved to be a total fabrication, other authors published "Baron Munchausen's Narrative of His Marvelous Travels and Campaigns in Russia". In 1951, Dr. Richard Asher described a disorder where patients fabricated histories, feigned illnesses, and deceived multiple care takers, heralding the birth of Munchausen Syndrome. In 1977, Meadow described Munchausen Syndrome By Proxy (MSBP), with children as the primary victims.

A review of the literature reveals that the perpetrator is often the natural mother of the child, with a high degree of intellect and often some medical training. The perpetrator alternates between acceptance and outrage towards the disease process, and will enlist medical personnel as unknowing accomplices in the investigation of the complaint. The characteristics of MSBP include either simulated or, in most cases, actual illness which is created by a caretaker with access to the child. Repetitive visits to medical facilities often prompt complex medical workups. Perpetrator denial is common. Most importantly, symptoms will abate in the absence of the perpetrator.

The toxicologic literature is filled with case reports of patients with Munchausen Syndrome By Proxy, as contained in the following table:

REPORTED CASES FROM THE LITERATURE

AGE (mo)	*SEX*	*PRESENTATION*	*AGENTS*	*OUTCOME*
36	F	Apnea	Pepper	Death
19	M	Prolonged sleep	Phenothiazines	Survival
6	F	Hypoglycemia	Salicylates	Survival
30	M	Vomiting, hypernatremia	Table salt	Survival
4	M	Seizure, hyponatremia	Diluted formula	Survival
18	M	Coma, hematemesis	Pine Oil	CNS damage
48	F	Fever, irritability	Vitamin A	Survival
56	F	Fever, recurrent infection	Dirty IV fluids	Survival
22	F	Polyuria, glucosuria	Glucose	Survival
84	M	Coma, apnea	Imipramine	Survival

Demographics of MSBP cases demonstrate that 84% of symptoms will occur within the hospital proper, and many patients will suffer from other forms of child abuse as well. In addition, sibling deaths have been reported. Of interest, Munchausen Syndrome is present in nearly 10% of the perpetrators.

Warning signs of MSBP include unexplained persistent or recurring illness, signs and symptoms that do not make sense, symptoms that magically disappear in the mother's absence, variable levels of maternal concern, and the presence of a fascinoma in general.

Disposition of the MSBP patient includes first and foremost separation of the child from the perpetrator. The clinician must perform an educated toxicologic workup. In many cases occult surveillance may be necessary to unearth the diagnosis. Most importantly, the clinician is cautioned to keep an open mind; nothing is too far fetched.

REFERENCES

Rosenberg DA. Web of deceit: Munchausen syndrome by proxy. Child Abuse and Neglect. 1987; 11: 547-563.

Dine MS. Intentional poisoning of children- an overlooked category of child abuse. Pediatrics. 1982; 70: 32-35

Contributed by R. Cantor, M.D.

TOX TRIVIA:

1. What was the recent toxin that caused an epidemic of renal failure in Haiti by being a contaminant in liquid acetaminophen?
2. The "mad hatter" was poisoned by?
3. When was the first Poison Control Center established?
4. What was the toxin responsible for "St. Anthony's Fire"?

CLINICAL TOXICOLOGY PEARLS:

1. Digoxin exposed patients may have depressed ST segments on ECG known as Salvador Dahlia's Mustache.
2. TCA exposed patients may have a rightward axis deviation of the terminal 40 msec of the QRS complex on ECG.
3. neither of the above infer toxicity, only exposure.

NEWS BULLETINS:

Congratulations to our newly Certified Poison Information Specialists!!!!

TOX TRIVIA ANSWERS:

1. Diethylene glycol
2. Mercury
3. 1953
4. Ergots

HISTORICAL "MATCHING" TIDBITS ANSWERS:

1. b
2. c
3. a
4. d